Remarks/Arguments

Prior to the present amendment, claims 1-27 were pending in this application, earlier submitted claim 28 apparently not having been entered. Claims 5-10 and 12-27 were withdrawn from consideration, while claims 1-4 and 11 were rejected. As part of the present response, claims 1 and 3 have been amended, and claims 4-27 have been canceled. The amendments include correction of an obvious typographical error, and incorporate subject matter into the pending claims from claims now canceled. The amendments do not add new matter.

It is emphasized that the non-elected claims have been canceled merely to be fully responsive to a final Office Action, as required by 37 CFR 1.144. Should the finality of the Office Action and/or of the restriction requirement be withdrawn, as currently requested, Applicant retains the right to reintroduce some or all of the claims canceled with the present amendment.

Request to Withdraw the Finality of the Rejections

It is submitted that the finality of the present Office Action, including the finality of the restriction requirement, is premature and should be withdrawn.

The Office Action is confusing and inconsistent in that the Examiner's response to Applicant's arguments concerning unity of the invention are based on the original, unamended claims, while the rest of the rejections appear to reflect the amendments submitted with Applicant's response of September 30, 2004.

In addition, Applicant, despite a specific request, was denied the opportunity to discuss the earlier rejections during a telephonic or personal interview, "due to the presence of many complex, unsolved issues." Applicant's representative requested the interview exactly to facilitate the resolution of such unsolved issues. Under 37 C.F.R. 1.133, the only time when interviews concerning the patentability of pending inventions are not held is before the issuance of the first Office Action. This was not the case here. As a result, Applicant is placed in the position of having to argue "complex, unsolved

issues" in response to a final Office Action, when such arguments are often not considered on their merits, necessitating the filing of a Continued Prosecution Application. In order to avoid such inequitable outcome, the Examiner is respectfully requested to withdraw the finality of the present Office Action.

Restriction

Applicant notes the finality of the restriction requirement, but requests reconsideration both of the finality and the requirement itself for the reasons set forth below.

The Examiner has failed to take into account the claim amendments submitted with Applicant's response of September 30, 2003 when assessing the unity of the invention, stating that "the amendment of claim 1 in response of 09/30/03 does not affect the restriction requirement, since the restriction requirement is based on originally presented claims." Accordingly, the Examiner's rebuttal of Applicant's previous traverse is replete with references to original claim 1, and language present in or missing from original claim 1, which leads to the conclusion that WO 96/02642A1 anticipates the claimed method, "because the method will inherently lead to the claimed effects."

The Examiner's approach is legally incorrect. Applicant is fully entitled to rebut a restriction requirement by amending the claims, and argue that, irrespective of whether the restriction requirement based upon the original claims was valid or invalid, it should be withdrawn in view of the claim amendments. Indeed, since the claim amendments submitted with Applicant's response of September 30, 2003 have been entered, the references in the Examiner's arguments to earlier claim language have no relevance to the question whether the amended claims should be subject to a lack of unity rejection.

Applicants, again, submit that the restriction requirement in the present case contravenes the provisions of PCT Rules 13.1-13.3, and should be withdrawn. To avoid repetitions, Applicant's related arguments from the response filed on September 30, 2003 are hereby expressly incorporated by reference.

The Examiner is respectfully requested to reconsider and withdraw the, now final, restriction requirement as it applies to the pending claims. Should the Examiner maintain the requirement, Applicant specifically retains the right to seek review via petition to the Commissioner.

Rejection under 35 USC 112, second paragraph, new rejection

Claims 1-4, and 11 were rejected as "indefinite" for the presence of a typographical error in claim 1. Since the error has been corrected, the rejection is believed to be moot, and should be withdrawn.

Rejection under 35 USC, first paragraph, new matter, new rejection

Claims 3-4 were rejected under 35 USC 112, first paragraph, "as failing to comply with the enablement requirement." According to the rejection, the specification "does not disclose a method for inducing growth inhibition or apoptosis in a population of cells in which mdm2 is not overexpressed, comprising administering an agent that disrupts the binding of p53 and mdm2, wherein said agent comprises a peptide having an amino acid sequences that 'consists of' 'a variant or a portion of human p53', which has the property of binding to mdm2."

The basis for this rejection is unclear for several reasons. First, the title of the rejection appears to indicate that the rejection is based on alleged presence of "new matter" in the rejected claims, while the reasoning is based on alleged lack of enablement. Secondly, the Examiner sets forth no specific reasons why the rejected claims would not be enabled. The law is clear that the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. (See, e.g. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Only after a prima facie case of lack of enablement has been established does the burden of rebuttal shift to the applicants. In the present case, the Examiner has not set forth any reasonable basis for the rejection.

Nonetheless, claim 4 has been cancelled, and Applicant submits that claim 3, which includes the recitations of the phrase "a portion of human p53" in combination with additional structural and functional features, is enabled. Accordingly, the withdrawal of the present rejection is respectfully requested.

Rejection under 35 USC 112, first paragraph, enablement

Claims 1-4 and 11 were rejected under 35 USC 112, first paragraph for alleged lack of enablement for essentially the same reasons as set forth in the previous Office Action. Claims 4 and 11 have been canceled. The rejection of the remaining claims, as currently amended, is respectfully traversed.

The Examiner argues that one "cannot extrapolate from increased transcriptional activity of p53 in transfected breast tumor cells with growth inhibition or apoptosis of a population of cells in which mdm2 is not overexpressed, or cancer cells in which mdm2 is not overexpressed, because the particular cellular outcome in response to activated p53 depends on cell type, cellular context and extracellular signals, and that in some cases p-53 mediated apoptosis can be inhibited by the presence of survival factors, including various cytokines, as taught by Haupt et al., of record."

Without acquiescing to the rejection as it applied to the unamended claims, or the reasoning underlying the rejection, the claims have been amended to refer to cancer cells. Applicant submits that extrapolation from breast cancer cells to cancer cells in general would be accepted by one skilled in the art as fully appropriate. In addition, it is noted that, when making a lack of enablement rejection, the burden is on the Examiner to establish that it is "more likely than not" that the rejected claims are not enabled. The citation of a reference showing that p53-mediated apoptosis can be inhibited by survival factors, when viewed against the totality of evidence, including WO 93/20238, WO 96/02642 and their US equivalents, does not meet this evidentiary burden. Indeed, the Examiner's refusal to give sufficient weight to the contents of this PCT publications and

US patent No. 6,153,391 is improper. The presence or absence of the indicia of patentability should be considered against the prior art as a whole, of which these patent publications are an important part. The Examiner's remark that "different applications are different and the patenting of US 6,153,391 does not apply to the instant application," is irrelevant. The '391 patent was not cited in Applicant's response of September 30, 2003 to argue that the present application should be allowed since the '391 patent was allowed, rather was relied on to establish general knowledge in the art, which is an important part of the assessment of enablement.

In view of Applicant's earlier arguments, which are hereby expressly incorporated by reference, the current claim amendments, and the present arguments, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Rejection under 35 USC 112, first paragraph, scope

(1) Claims 1-4, and 11 were rejected under 35 USC 112, first paragraph for alleged lack of enablement for using, in the claimed methods, an agent or a variant of p53, that disrupts the binding of p53 and mdm2, for reasons of record.

Claims 4 and 11 have been canceled, without prejudice. The rejection of claims 1-3 is respectfully traversed.

It is unclear how this "scope" rejection differs from an "enablement" rejection, as the rejection set forth above. Regardless, the agents used in the pending claims now characterized by a combination of specific structural and functional features, and are, therefore, believed to meet the enablement requirement of 35 USC, first paragraph. Accordingly, Applicant request the withdrawal of the present rejection.

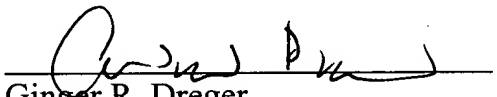
(2) Claims 1-4, and 11 were rejected for alleged lack of enablement for a method that targets cells in which mdm2 is not overexpressed, or cancer cells in which mdm2 is not overexpressed.

First of all, the claims are now specifically drawn to cancer cells, therefore, the Examiner's comments on normal cells no longer apply. Secondly, the Examiner provided no specific reasons why one could not extrapolate from the behavior of one cancer cell that does not overexpress mdm2 (e.g. a breast cancer cell) to the behavior of other cancer cells that do not overexpress mdm2. The general statement that "different cancer cells have different etiology and characteristics, and the responses of different cancer to a therapeutic agent are not necessarily the same" does not suffice as a proper support for a rejection. The Examiner is respectfully requested to withdraw the present rejection or, if the rejection is maintained, provide specific reasons why in the present case one skilled in the art would not be able to practice the present invention with regard to all cancers that do not overexpress mdm2, without undue experimentation.

All claims pending in this application are believed to be in prima facie condition for allowance, and an early action to that effect is respectfully solicited. Should the Examiner maintain any of the rejections, she is, again, respectfully requested to contact the undersigned to schedule a telephonic or personal interview.

Sincerely,

Date: July 13, 2004



Ginger R. Dreger
Reg. No. 33,055

Heller Ehrman White & McAuliffe, LLP
Customer No. 25213
275 Middlefield Road
Menlo Park, CA 94025
Tel: 650/324-7000
Fax: 650/324-0638